

REMARKS

Status of the Claims

Claims 38-45 and 113-122 are pending in the present application. Claim 38 has been amended as described elsewhere herein. New claims 122 has been added. Support for this claim is found in the original specification and claims as filed including, for example, original claim 38 and lines 13-18 of the specification. No new matter has been added by way of amendment. Reconsideration and withdrawal of the rejections are respectfully requested.

The Sequence Listing

Applicants have amended the application to enter the sequence listing filed on January 20, 2006.

The Specification

The Examiner correctly noted that the amendments to the specification listed in the amendment mailed January 20, 2006, contained certain informalities. In the Amendments to the Specification, Applicants have presented corrected versions of the amendments at issue.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 38 and dependent claims 39-45 and 114-120 have been rejected under 35 U.S.C. § 112, second paragraph, on the grounds that the phrases "the large pocket volume of the GR polypeptide structure," "the A-subunit of said expanded binding pocket," "the B-subunit of said expanded binding pocket," and "the corresponding subunit of the GR/dexamethosone structure" is unclear. The rejection is respectfully traversed for the reasons described below.

The *Manual of Patenting Examining Procedure (MPEP)* states that "[t]he test for definiteness under 35 U.S.C. 112, second paragraph is whether 'those skilled in the art

would understand what is claimed **when the claim is read in light of the specification.**" *MPEP* § 2173.02, citing *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 805 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986) (emphasis added). Claim 38 meets this requirement because the specification describes the large pocket volume of the GR polypeptide expanded binding pocket, and the A- and B- subunits of the expanded binding pocket, and identifies the corresponding subunits of the GR/dexamethasone complex. See, for example, lines 20-25 of page 13, lines 1-8 of page 33, and Figures 5A, 5B, 6A, 6B, 7A, 7B, 8A, 8B. Claim 38 has also been amended to clarify that the large pocket volume referred to in part (b) of claim 38 is the expanded binding pocket volume. In view of the descriptions of these phrases provided in the description, one of skill in the art, when reading claim 38 in light of the supporting specification, would understand what is encompassed by the claim.

Claim 38 and dependent claims 39-45 and 114-120 have been rejected under 35 U.S.C. § 112, second paragraph, on the grounds that the phrases "the large pocket volume of the GR polypeptide structure," "the A-subunit of said expanded binding pocket," "the B-subunit of said expanded binding pocket," and "the corresponding subunit of the GR/dexamethasone structure" lack antecedent basis in the claim. The rejection is respectfully traversed, because the phrases at issue do not refer back to an earlier recitation of the same element in the claim, but rather to inherent components of elements recited earlier in the claim. The *MPEP* provides that "[i]nherent components of elements recited have antecedent basis in the recitation of the components themselves." *MPEP* § 2173.02, citing *Bose Corp. v. JBL, Inc.*, 274 F.3d 1354, 1359, 61 USPQ2d 1216, 1218-19 (Fed. Cir. 2001). Accordingly, claim 38 and dependent claims 29-45 and 114-120 meet the requirements of 35 U.S.C. § 112, second paragraph.

Claim 38 and dependent claims 39-45 and 114-120 have been rejected under 35 U.S.C. §112, second paragraph, on the grounds that these claims are unclear because they refer to the GR/dexamethasone structure having the coordinates set forth in Table 3, but these coordinates correspond to a GR/dexamethasone/TIF2 ternary complex.

Claim 38 has been amended for the purpose of clarifying this issue, thereby obviating the rejection.

Claims 38 and dependent claims 39-45 and 114-120 have been rejected under 35 U.S.C. §112, second paragraph, on the grounds that these claims are indefinite for reciting that the pocket volume of the A-subunit of the expanded binding pocket is increased by about 58 cubic angstroms in comparison with the corresponding subunit of the structure having the coordinates set forth in Table 3, and the pocket volume of the B-subunit of the expanded binding pocket is increased by about 138 cubic angstroms in comparison with the corresponding subunit of the structure having the coordinates set forth in Table 3. The Examiner states that the use of the term "about" is indefinite. Applicants respectfully traverse the rejection. In previous cases, the term "about" has been held to be clear, but flexible. See *MPEP* § 2173.05(b), citing *Ex parte Eastwood*, 163 USPQ 316 (Bd. App. 1968) and *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). Furthermore, the specification provides an extensive description properties of the GR expanded binding pocket. See, for example, lines 1-6 of page 33, lines 1-20 of page 35, of page 35, and Figures 4,5A, 5B, 6A, 6B, 7A, 7B, 8A, 8B, 9-16, lines 18 of page 33. Accordingly, one of skill in the art would recognize the metes and bounds of the expanded binding pocket recited in claim 38.

In view of the above arguments and amendments, all grounds for rejection under 35 U.S.C. § 112, second paragraph, have been obviated or overcome. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

The Rejections Under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Claim 38 and dependent claims 38 and 115 and their respective dependent claims have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that they contain new matter. The rejection is respectfully traversed.

The Examiner argues that the specification does not provide support for the the recitation in claim 38 of an expanded binding pocket where the pocket volume of the A-

subunit of said expanded binding pocket is increased by about 58 cubic angstroms in comparison with the corresponding A-subunit of the structure having the coordinates set forth in Table 3, and the pocket volume of the B-subunit of said expanded binding pocket is increased by about 138 cubic angstroms in comparison with the corresponding B-subunit of the structure having the coordinates set forth in Table 3. The Examiner appears to acknowledge that the specification contains support for language of the amendment, but states that the specification "fails to support a model for any liganded/unliganded GR polypeptide structure having any structural coordinates." Applicant respectfully requests further clarification of the basis for the rejection. Lines 7-15 of page 31 of the specification state:

As used herein, the term "expanded binding pocket" means an NR ligand binding pocket in which atoms in the protein have shifted so as to increase the volume available to the ligand. The GR/FP structure disclosed in Table 2 provides an example in which, in the A-subunit, the pocket volume increases by approximately 58 cubic angstroms compared with the corresponding subunit of the GR/Dex structure, as described in Table 3, and in which, in the B-subunit, the pocket volume increases by approximately 138 cubic angstroms compared with the corresponding subunit of the GR/Dex structure.

Lines 5 and 6 of page 33 also provide support for claim 38 as amended. Accordingly, the language of claim 38 as amended is fully supported by the specification.

According to the *MPEP*, "[t]he examiner has the initial burden of presenting by the preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *MPEP* § 2163.04, citing *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). In the present case, the specification demonstrates that the applicants were in possession of a GR structure having an expanded binding pocket, including a GR structure having an expanded binding pocket where the pocket volume of the A-subunit of said expanded binding pocket is increased by about 58 cubic angstroms in comparison with the corresponding A-subunit of the structure having the coordinates set forth in Table 3, and the pocket volume of the B-subunit of said expanded binding pocket is increased by about 138 cubic angstroms in comparison with the corresponding B-subunit of the

structure having the coordinates set forth in Table 3. Accordingly, one skilled in the art would recognize in the disclosure a description of the invention defined by claim 38.

New claim 115 has been rejected under 35 U.S.C. §112, first paragraph on the grounds that it contains new matter. The rejection is respectfully traversed. Support for this claim is found in original claims 39 and 44.

The Examiner has rejected claims 38-43, 45, 114, and 120 under 35 U.S.C. § 112, first paragraph on the grounds that these claims are not supported by a sufficient written description. The rejection is respectfully traversed for the reasons described below.

The Examiner argues that the written description of the invention of claims 38-43, 45, 114, and 120 is insufficient because the applicants have disclosed only one working example of a GR structure having an expanded binding pocket, and this is insufficient to describe the recited genus of GR structures. However, the genus of structures encompassed by claim 38 is not described solely on the basis of a single working example. In fact, the applicants have identified the structural features that characterize the expanded binding pocket, and these structural features are recited in the claim. According to the *MPEP*:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice [], reduction to drawings [], or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus [].

MPEP § 2613, citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 (emphasis added). In the present case, written description of the invention of claim 38 is demonstrated by two examples of the actual reduction to practice of the method recited in claim 38, by numerous drawings of the expanded binding pocket recited in claim 38, and by a recitation of the relevant structural features that characterize this expanded binding

pocket. Accordingly, the Office has not established a *prima facie* case showing that at the time the application was filed one skilled in the art would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed.

Claims 38-43, 45, 114, and 120 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the claimed invention does not provide sufficient enablement to allow one of skill in the art to make and use the claimed invention. The rejection is respectfully traversed for the reasons described below.

In the Amendment filed January 20, 2006, the applicants summarized the extensive guidance provided in the specification for making and using the claimed invention, and demonstrated that undue experimentation would not be required to practice the claimed methods in view of the breadth of the claims (which are directed to methods of identifying GR modulators using a GR polypeptide structure having an expanded binding pocket having defined structural characteristics), the amount of direction provided in the specification (which provides extensive guidance for practicing the methods as described in the previous Amendment), the presence of multiple working examples, the prior art (which teaches methods for designing and modeling ligands based on the three-dimensional structure of the ligand binding site), and the high level of skill of those in the art.

However, the Examiner argues that undue experimentation would be required to practice the invention because the specification provides only a single working example of coordinates that have an expanded binding pocket as recited in claim 38. According to the *MPEP*, "[t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." *MPEP* § 2164.02. In the Office Action, the Examiner argues that undue experimentation would be required to identify additional GR polypeptide structures comprising an expanded binding pocket. However, the only evidence offered to support this argument is the

applicants' specification at line 23 of page 7 through line 19 of page 8. This section of the specification is directed to making predictions of GR structure in the absence of crystallographic data. In contrast, the applicants have now resolved the structure of a GR polypeptide complex having an expanded binding pocket, and have described the structural features which characterize the expanded binding pocket. Claim 38 encompasses the use of these structural features to identify GR modulators. Accordingly, the section of the specification cited by the Examiner is not relevant to the enablement of the instant claims, and a *prima facie* case of non-enablement has not been established.

Claim 45 has been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that it is not enabled because the specification provides only a single method of performing an assay for ligands that modulate GR activity. The rejection is respectfully traversed. Methods for assaying GR activity are well known to those of skill in the art. Furthermore, the Federal Circuit has held that the specification need only teach one mode of making and using the claimed invention to satisfy the enablement requirement. *Engel Industries v. The Lockformer Co.*, 20 USPQ2d 1300, 1304 (Fed. Cir. 1991) *Johns Hopkins Univ. v. Cellpro, Inc.*, 47 USPQ2d 1705 (Fed. Cir. 1998), and *Durel Corp v. Osram Sylvania Inc.* 59 USPQ2d 1238 (Fed. Cir. 2001). Accordingly, claim 45 meets the requirements for enablement as set forth in the relevant Federal Circuit holdings.

In view of the above arguments and amendments, all grounds for rejection under 35 U.S.C. § 112, first paragraph, have been overcome or obviated. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

The Rejection under 35 U.S.C. § 103 Should be Withdrawn

The Examiner has withdrawn the previous rejection under 35 U.S.C. § 103. However, the Examiner has newly rejected claims 38-45 and 114-120 under 35 U.S.C. § 103 on the grounds that recitation of atomic coordinates in these claims should not given patentable weight in construing the claims, and that claims 38-44 and 114-120

are therefore obvious in view of Apolito *et al.* (WO 03/015692), Gillner *et al.* (WO 00/52050), and claim 45 is obvious in view of Apolito *et al.*, Gillner *et al.*, and Hogger *et al.* (1994) *Steroids* 59(10):597-602. The rejection is respectfully traversed for the reasons described below.

The Examiner argues that the recitation of structural coordinates in claims 38-45 and 114-120 constitutes nonfunctional descriptive matter and that these claim limitations should not be considered in construing the claims. No reasoning is presented to support this assertion. Applicants note that the present invention is not directed to a mathematical algorithm or computer program. Rather, the instant claims directed are to methods of using of novel GR expanded binding pocket structure in the design of GR modulators. According to *MPEP*, nonfunctional descriptive material is material "that cannot exhibit any functional interrelationship with the way in which computing processes are performed." *MPEP* § 2106. In the instant case, the atomic coordinates recited in the claims describe structural information about the novel GR expanded binding pocket structure, and this structural information is used in the claimed method to identify GR modulators. Accordingly, the structural coordinates recited in the claims represent a functional element of the claimed methods, and these limitations should be considered in construing the claims for the purposes of determining patentability.

In the rejection, the Examiner cites *In re Gulack*, 703 F.2d 1381, 217 USPQ 401 (Fed. Cir. 1983) and *In re Ngai* 70 USPQ2d 1862 (Fed. Cir. 2004) in support of the rejection. However, the present claims are factually distinguishable from the subject matter of the claims at issue in *Gulack* and *Ngai*. In *Gulack*, the claims were directed to a mathematical device comprising an endless band imprinted with a specified array of digits. The issue before the Federal Circuit in *Gulack* was whether the content of the printed matter on the band should be given patentable weight in determining whether the claimed device was obvious in view of the prior art. The Examiner and the USPTO Board of Appeals ("the Board" had failed to consider the printed matter in determining the patentability of *Gulack*'s claims, and had found them unpatentable on the grounds

on the grounds that they were obvious. The Federal Circuit reversed the Board, stating "[d]ifferences between an invention and the prior art cannot be ignored merely because those differences reside in the content of the printed matter." *Gulack*, 703 F.2d at 1385, 217USPQ at 403.

In *Ngai*, the issue before the Federal Circuit was whether an inventor could patent a kit composition, where the only difference between the prior art and the claimed kit was the content of instructions included in the kit. The court found that the instructions did not depend on the kit, and the kit did not depend on the instructions; therefore, the addition of the instructions did not make the kit patentable. The Court held that *Ngai* was entitled to a patent on his new method, but was not entitled to a patent on the kit.

In contrast with *Gulack* and *Ngai*, the present claims are not directed to a composition comprising printed matter, where the printed matter must be given patentable weight in order to distinguish the invention over the prior art. Rather, the present claims are directed to a method of designing modulators of GR based on the novel structure of the GR expanded binding pocket. The claims rely on the novel structure of the expanded binding pocket, rather than a particular array of printed matter to distinguish the invention from the prior art. Accordingly, the holdings of *Gulack* and *Ngai* are inapposite to the patentability of the present claim and do not support the claim construction set forth in the Office Action.

The atomic coordinates recited in claims 38-44 and 114-120 describe structural information about the novel GR expanded binding pocket structure, and this structural information is used in the claimed method to identify GR modulators. Accordingly, the atomic coordinates are functional material should be considered when construing the scope of the claims. *Apolito et al.*, *Gillner et al.*, and *Hogger et al.*, either alone or in combination, neither teach nor suggest the all of the limitations of claims 38-44 or 114-120 when properly construed.

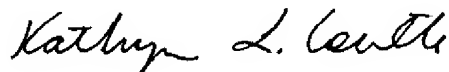
In view of the above arguments, all grounds for rejection under 35 U.S.C. § 103 have been overcome. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

It is believed that the current application is now in condition for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, an interview would expedite prosecution, the Examiner is invited to call the undersigned.

Applicants believe that no fees are due in connection with the filing of this paper other than those specifically authorized herein. However, should any other fees be deemed necessary to effect the timely filing of this paper the Commissioner is hereby authorized to charge such fees to Deposit Account No. 07-1392.

Respectfully submitted,



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